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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,854	07/23/2003	Andre Delacourte	11362.0039.NPUS01	9442

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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
05/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/625,854	DELACOURTE ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,34-37,40-43,56-61 and 63* is/are pending in the application.

4a) Of the above claim(s) *37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,34-36,40-43,56-61 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 23, 2007 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed February 23, 2007 is acknowledged. Claims 1-25, 27-33, 38, 39, 44-55, 62 are cancelled. Claims 26, 34-37, 40-43, 56-61 and 63 are pending. Claim 37 is withdrawn from consideration as directed to nonelected inventions. Claims 26, 34-36, 40-43, 56-61 and 63 are under examination in light of Aβ (4-42) and Aβ (5-42) in this office action.

Claim Rejections/Objections Withdrawn

3. The rejection of claims 29, 39, 40, 55, 60 and 63 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement is withdrawn in response to Applicant's amendment to the claims and cancellation of claims 29 and 39.

The rejection of claims 26, 29, 30-42, 55-63 under 35 U.S.C. 112, second paragraph, for being indefinite because of the recitation "particular" is withdrawn in

response to Applicant's amendment to the claims and cancellation of claims 29, 30, 33, 38, 39, 55 and 62.

Claim Rejections/Objections Maintained

Claims 34-36 and 43 were under examination at the first non-final action. Applicant may cancel a claim but may not withdraw it from consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claims 26, 34-36, 40-43, 56-61 and 63 under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement is maintained for reasons of record in the previous office action.

Applicant argues that amended claims are directed to early identification of Aβ variants in living patients, which aids to determine whether a person is susceptible to or at risk of diseases associated with Aβ formation. Applicant argues that the claims are enabled because the specification teaches how to detect and identify modified Aβ42 variants in dead or living patients with a disease associated with Aβ formation. Applicant argues that amended claim 26 is enabled for determining whether a mammal is susceptible to a disease associated with Aβ formation because different Aβ42 variants can be detected in CSF of patients and in different stages of AD as in specification. Applicant argues that claim 60 is enabled because the examiner did not include claim

60 in the rejection under 112 first paragraph, lack of enablement. Applicant argues that should claim 60 is allowable, claim 43 is ready for examination. Applicant argues that claim 43 is enabled because claim 43 is directed to Aβ8-42, which can be detected in CSF of AD patients and S0 controls. Applicant argues that controls are patients with no pathology (S0) and patients with PHF-tau pathology but no clinical impairment and they are not inconsistent because S0 cannot be detected with any Aβ42 peptides. Applicant states that the argument is supported by Dr. Vanmechelen's declaration. Applicant argues that claim 57 is enabled because Aβ4-42 can be detected in CSF of infraclinial and clinical AD patients and that the argument is supported by Dr.Vanmechelen's declaration.

5. Applicant's arguments have been fully considered but they are not persuasive. In response to Applicant's arguments with regard to amended claims being enabled because amended claims are directed to determining susceptibility and the specification teach how to detect and identify the variants, the examiner asserts that the amended claims are not enabled based on the disclosure. Based on the disclosure, Applicant is only enabled for detecting Aβ5-42, Aβ2-42 or other Aβ42 variants with an N-terminal truncation or post-translation modification in CSF of patients with AD. Applicant is also enabled for detecting Aβ8-42, Aβ11-42 and Aβ10-42 in S0 controls. However, the claims are directed to predicting whether a person is susceptible to or at risk of a disease associated with Aβ formation. Since certain forms of Aβ42, such as Aβ8-42, Aβ11-42, Aβ10-42 variants, can also be detected in controls, they do not distinguish between the controls and AD. Thus, not all forms of Aβ42 variants are suitable for

distinguishing controls and AD. In addition, there is no guidance as to what levels of Aβ42 variants are different between controls and AD and no guidance as to distinguish the levels of Aβ42 variants between no disease and later developing a disease. There is no guidance as to what specific N-terminal truncated Aβ42 fragments change and how much change would be considered indicative of a risk of disease. Thus, based on the disclosure, a skilled artisan still cannot determine whether a person is at risk of diseases associated with Aβ formation by detecting Aβ42 or even specific Aβ42 variants such as Aβ5-42, 4-42, 8-42. In addition, the data shown in the specification and declaration are derived from patients suffering from Alzheimer's disease rather than patients who are free of Alzheimer's disease and later develop Alzheimer's disease. Thus, it is unpredictable whether any forms of Aβ42 variants can be used as an indicator of whether a patient is susceptible to or at risk of the diseases. Applicant has not provided any specific information to predict which one of us would develop a disease associated with Aβ formation/aggregation or which one of us would not based on the claimed method. The specification has not taught what would be different in normal people and people at risk for AD in what level of Aβ42 variants

6. In response to Applicant's argument that claim 60 is enabled, it is noted that claim 60 was erroneously excluded in the last sentence of rejection. Claim 60 is not enabled for the reasons as set forth above. In addition, Applicant is not enabled for detecting Aβ5-42 in all types of body fluid samples since the expression of Aβ5-42 can only be detected in CSF. In addition, the expression levels of different fragments of Aβ are different in different tissues. For example, Aβ5-42 or other Aβ peptides cannot be

detected in saliva, which is also a body fluid sample. Furthermore, the plasma level of Aβ does not correlate with the level of Aβ in CSF as shown in the prior art (see p. 102, abstract, Mehta et al. Neurosci. lett. 2001. 304: 102-106). Thus, Applicant fails to provide sufficient guidance as to enable one of skill in the art to practice the claimed method as in claim 60.

7. In response to Applicant argument with regard to claim 43, it is noted that claim 60 is not allowable. Thus claim 43 is withdrawn from consideration. In addition, Aβ8-42 as in claim 43 can be detected in both normal and AD indicating that Aβ8-42 is not unique in AD patients. Thus Aβ8-42 can cannot be used as an indicator of determining whether a person is susceptible of Aβ associated diseases because a skilled artisan cannot determine what levels of change would be considered as a prognostic indicator of determining whether a person is susceptible to or at risk of the disease.

8. In response to Applicant's argument with regard to controls, it is noted that Aβ8-42, Aβ10-42 and Aβ11-42 can be detected in S0 controls as shown in declaration (Appendix 3, p. 2) and specification (p. 74, table 8). Applicant fails to distinguish the levels of these Aβ42 variants in controls from the levels in AD patients. In addition, since certain forms of Aβ42 variants can be detected in controls, there is no guidance as to distinguish what specific fragments of Aβ42 and what levels of Aβ42 variants would be considered as real controls in order to support the argument. A skilled artisan cannot use the levels of these Aβ42 variants to predict whether a person is susceptible to or at risk of the diseases associated with Aβ formation.

8. In response to Applicant's argument with regard to claim 57, it is noted the detection of Aβ4-42 in CSF of AD patients is not an indicator of a person being at risk of a disease associated with Aβ formation. Although Applicant is enabled for detecting Aβ4-42 in CSF of AD patients, a skilled artisan still cannot predict whether a person is susceptible to or at risk of the diseases since Aβ4-42 is found in patients who have been diagnosed as AD rather than patients who are free of AD symptoms and later develop AD symptoms.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is

(571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
April 30, 2007

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER